

08/28/2008

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. (currently amended) A method for determining the sequence of a nucleic acid molecule, comprising the steps of:

a) providing a single-stranded form of said nucleic acid molecule;

b) hybridizing a primer to said single stranded form of said nucleic acid molecule to form a template/primer complex;

c) ~~enzymatically~~ extending the primer by reading the result of the primer extension and preparing for a next cycle by enzymatically extending the primer by the addition of a polymerase and a mixture of at least one nucleotide and at least one labeled derivative of the at least one nucleotide, wherein the at least one labeled derivative of the at least one nucleotide comprises a label linked to the nucleotide via a cleavable link and wherein the amount of labeled derivative of the at least one nucleotide in said mixture of the at least one nucleotide and the labeled derivative of the at least one nucleotide is within the range of 1-50 mole-%; determining the type of nucleotide added to the primer after extending said primer and neutralizing the label by adding a label-interacting agent or by bleaching after determining the type of nucleotide

added to the primer before any additional primer extensions can be added; and

~~— d) determining the type of nucleotide added to the primer and thereafter neutralizing the label by adding a label-interacting agent or by bleaching; and~~

[[e]] d) repeating ~~steps~~ step c) ~~to d)~~ at least once.

2. (previously presented) The method according to claim 1, in which the amount of labelled derivative of the at least one nucleotide in said mixture is within the range of 5-50 mole-%.

3. (previously presented) The method according to claim 1, in which the amount of labelled derivative of the at least one nucleotide in said mixture is within the range of 10-50 mole-%.

4. (previously presented) The method according to claim 1, wherein the single-stranded form of said nucleic acid molecule is attached to a carrier.

5. (currently amended) The method according to claim 4, wherein a mechanism for attachment to the carrier is a specific binding to a hydrophobic compound, an oligonucleotide, an antibody or a fragment thereof, a protein, a peptide, an intercalating agent, biotin, streptavidin or avidin; or [[b)]]

covalent coupling using an amino-linker and an epoxy-treated carrier.

6. (previously presented) The method according to claim 4, wherein the carrier is selected from the group of a gel, a solid or porous bead, a surface or a fiber.

7. (canceled)

8. (previously presented) The method according to claim 1, in which the label is neutralized by bleaching and the bleaching is performed by photo-bleaching.

9. (canceled)

10. (previously presented) The method according to claim 1, in which the link between a fluorophore and nucleotide is a disulfide bond.

11. (previously presented) The method according to claim 10 in which the cleavage is performed by the addition of a reducing agent, thereby exposing a thiol group to provide an exposed thiol group.

12. (previously presented) The method according to claim 10, in which the exposed thiol group is capped by a reagent.

13. (previously presented) The method according to claim 1, in which a linker between a disulfide bridge and the base is shorter than 8 atoms.

14. (previously presented) The method according to claim 1, in which step c) is performed at a pH below 7.

15. (previously presented) The method according to claim 1, in which the derivative of said nucleotide is a dideoxynucleotide or an acyclic nucleotide analog.

16. (currently amended) The method according to claim 1, wherein the label is neutralized with an agent and the agent is selected ~~from~~ from the group consisting of alkaline phosphatase, PPi-ase, apyrase, dimethylsulfoxide, polyethylene glycol, polyvinylpyrrolidone, spermidine, detergents, NP-40, Tween 20, Triton X-100; proteins that affect secondary structure of DNA, Single Stranded DNA Binding Protein (SSB) and a protein of Gene 32.

17-18. (canceled)

19. (new) A method for determining the sequence of a nucleic acid molecule, comprising the steps of:

a) providing a single-stranded form of said nucleic acid molecule;

b) hybridizing a primer to said single stranded form of said nucleic acid molecule to form a template/primer complex;

c) extending the primer by reading the result of the primer extension and preparing for a next cycle by a procedure that consists of:

i) enzymatically extending the primer by the addition of a polymerase and a mixture of at least one nucleotide and at least one labeled derivative of the at least one nucleotide, wherein the at least one labeled derivative of the at least one nucleotide comprises a label linked to the nucleotide via a cleavable link and wherein the amount of labeled derivative of the at least one nucleotide in said mixture of the at least one nucleotide and the labeled derivative of the at least one nucleotide is within the range of 1-50 mole-%;

ii) determining the type of nucleotide added to the primer;

iii) neutralizing the label by adding a label-interacting agent or by bleaching; and

after determining the type of nucleotide added to the primer before any additional primer extensions can be added; and

d) repeating step c) at least once.

20. (new) The method according to claim 19, in which the label is neutralized by bleaching and the bleaching is performed by photo-bleaching.

21. (new) The method according to claim 19, in which the link between a fluorophore and nucleotide is a disulfide bond.

22. (new) The method according to claim 21, in which the cleavage is performed by the addition of a reducing agent, thereby exposing a thiol group to provide an exposed thiol group.

23. (new) The method according to claim 21, in which the exposed thiol group is capped by a reagent.

24. (new) The method according to claim 19, in which a linker between a disulfide bridge and the base is shorter than 8 atoms.

25. (new) The method according to claim 19, in which step c) is performed at a pH below 7.

26. (new) The method according to claim 19, in which the derivative of said nucleotide is a dideoxynucleotide or an acyclic nucleotide analog.

27. (new) The method according to claim 19, wherein the label is neutralized with an agent and the agent is selected from the group consisting of alkaline phosphatase, PPI-ase, apyrase, dimethylsulfoxide, polyethylene glycol, polyvinylpyrrolidone, spermidine, detergents, NP-40, Tween 20, Triton X-100; proteins that affect secondary structure of DNA, Single Stranded DNA Binding Protein (SSB) and a protein of Gene 32.